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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,795	TRIEBEL ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31,34,35,37,38 and 41-63* is/are pending in the application.

4a) Of the above claim(s) *1-6,12,16-18,22-28,37,38 and 41-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *7-11,13-15,19-21,30,31,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendments filed 7-11-2002 (paper no. 14) is acknowledged and entered into the record. Claims 33,36,39, and 40 are canceled without prejudice. Claims 1-31, 41-63 are pending, claims 1-6, 12,16-18,22-29,37-38, and 41-63 are withdrawn from consideration as being drawn to non-elected claims, and therefore claims 7-11,13-15,19-21,30-31, and 34-35 are examined on the merits.

2. This application contains claims 1-6, 12,16-18,22-28,37-38, and 41-63 are drawn to an invention non-elected with traverse in Paper No. 11. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections Withdrawn

3. The rejection of claims 7 and 14 under 35 USC 112, second paragraph, as being indefinite, is **withdrawn**, in light of the amendments to the claims.

4. The rejection of claims 33 and 40 under 35 USC 112, first paragraph, as lacking enablement is rendered moot and is **withdrawn**.

Claim Rejections Maintained

5. The rejection of claims 11 and 13 under 35 USC 112, second paragraph, as being indefinite, is **maintained**. The arguments furnished by the applicant have been carefully considered but have not been found persuasive for the following reasons. Regarding claim 11, although the amendment partially clarifies the indefiniteness of the claim, the "element" encompassed by the claim still renders the claim indefinite because the metes and bounds encompassed by the term "element" can be virtually anything

that has those characteristics. Regarding claim 13, the peptide fragment has not been distinctly and definitely claimed. Although the peptide has been limited to the hsp70 protein, the actual fragment or portion claimed has not been distinctly claimed, therefore the metes and bounds of claim cannot be distinctly defined.

New Claim Rejections

Claim Rejections - 35 USC § 112

6. Claims 7-10, 13-14, 19-21, 30-31, and 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 7 and 35 are indefinite in the recitation of the term T-response because it is unclear whether the applicant intends to mean T-cell response. Applicant is advised to amend the claim language if it is the applicant intent to mean a "T cell response".

OK

8. Claim 19 is indefinite in the recitation of the phrase "mixture of peptide", because it is not known which peptides are to be included in the mixture therefore the metes and bounds of the claim cannot be determined.

OK

9. Claim 34 and 35 are indefinite in the recitation of the term ex situ and in situ because it is unclear as to the meanings of the terms. Regarding the term ex situ, it is unclear as to how vaccination to a patient is to be accomplished ex situ. Regarding the claim in situ, it is unclear as to how in situ administration is to be accomplished.

OK

10. Claims 11 and 13-14, 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. The written description in this case only sets forth the peptides encompassed by SEQ ID No: 1 and 2, and peptides that have naturally occurring amino acids, and therefore the written description is not commensurate in scope with the claims that read on peptide fragments of hsp70, peptides having at least 80% homology to the naturally occurring hsp70, nor are they commensurate in scope to peptide compounds that comprise elements.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of SEQ ID NO:1 and 2, the skilled artisan cannot envision the detailed structure of the encompassed by peptide fragments, peptides having 80% homology to that of naturally occurring hsp70 or peptide comprising elements. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The amino acid sequence itself or the element to which is being made part of the peptide sequence is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc.*

V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016. Although these court findings are drawn to DNA art, the findings are clearly applicable to the claimed proteins.

Furthermore, although drawn specifically drawn to the DNA art the findings of *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412) are clearly applicable to the instant rejection. The court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Support for peptide fragments, peptides having at least 80% homology to naturally occurring hsp70 is provided in the specification on page 5 and 7. However, no disclosure, beyond the mere mention of such fragments or homologous proteins are made in the specification. Furthermore, the written description of the type or types of elements to be inserted into the peptide is absent from the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only a peptide consisting of SEQ ID No: 1 and 2 meets the written description provision of 35 USC 112, first paragraph. If the applicant is able to over come the written description rejection set forth above for claim 8, a newly applied art rejection can be made.

Claims 11, 34 and 35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factors are the nature of the

invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed.

The nature of the invention: The claims of the instant invention are drawn to a compound comprising at last 8 amino acids from naturally occurring hsp, wherein the compound comprises at least one element other than a naturally occurring amino acid, and a method of immunizing to a subject a compound comprising a peptide either ex situ or in situ.

The state of the prior art and the predictability or lack thereof in the art: The art teaches that peptides used for the generation of an immune response to a tumor is often difficult and unpredictable in terms of its ability to generate a therapeutically effective immune elicitation. For example, Gaiger *et al* (Blood 2000 Aug 15;96(4):1480-1489) teach that a peptide derived from a tumor antigen had little effect in its ability to elicit a strong immune response (see page 1486 fig 10). Gaiger *et al* further attributed the inability of the peptides to elicit an immune response to the weak antigen recognition (see pg 1487)

The amount of direction or guidance present and the presence or absence of working examples: The working examples of the instant invention are drawn to methods of identifying mutants of hsp to be used as antigen recognition sites, production of antibodies, and peptide synthesis. However, nowhere in the specification does it teach peptide compounds that comprise additional elements, nor does it teach methods of ex

situ or in situ immunization with a peptide compound for the generation of T-cell responses.

The breadth of the claims and the quantity of experimentation needed: Because the instant specification has not taught one of skill in the art how to make peptide compounds encompassed by the claims, how to immunize a subject with a peptide compound ex situ or in situ and absent sufficient teachings in the specification to overcome the teachings of unpredictability found in the art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 7-10, 13, 19, 21, 30, 34 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Dragon *et al* (WO9002564-A). Claims 7-10, 13, 19, 21, 30, 34 and 35 are drawn to a peptide compound that comprises at least 8 consecutive amino acids of natural hsp70 sequence, wherein the peptide has at least 80% homology with amino acids between 286-294 of natural hsp70, wherein the amino acid at position 293 is chosen from isoleucine, leucine, valine, alanine, glycine, and phenylalanine, wherein the sequence is chosen from SEQ ID No: 1 and 2; a vector expressing a peptide

compound; a pharmaceutical compositions comprising peptide compounds, wherein the composition comprises a pharmaceutically acceptable vehicle wherein the composition is compatible with IV, subcutaneous, oral, or nasal administration; and a method of immunization comprising the administration of a peptide compound wherein the peptide comprises at least 8 consecutive amino acids of naturally occurring hsp70 and a peptide which comprises at least 8 consecutive amino acids of hsp70 having at least one mutation with respect to naturally occurring hsp70. Dragon *et al* teach a peptide that is at least 8 consecutive amino acids of natural hsp70 protien, wherein the peptide is at least 80% identical to naturally occurring hsp70 between 286-294, and wherein the amino acid at position 293 is a phenylalanine. Dragon *et al* teach a recombinant sequence of nucleic acids encoding a hsp70, wherein in the absence of any evidence to the contrary is a peptide that is at least 8 consecutive amino acids of naturally occurring hsp70; a pharmaceutical composition comprising at least 8 consecutive amino acids of naturally occurring hsp70, wherein the composition further comprises a pharmaceutical carrier which in the absence of any evidence to the contrary is compatible with IV, subcutaneous, oral, or nasal administration, and a method of administering a peptide having at least 8 consecutive peptides of naturally occurring hsp70 or a peptide of hsp70 having at least 8 consecutive peptides having at least one mutation with respect to naturally occurring hsp70.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 7-10, 13, 19-21, 30-31, 34 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dragon *et al* in view of Prakken *et al* (PNAS USA 1997 April; 94:3284-3289) and Costa MH *et al* (Appl Biochem Biotechnol 1998 Apr; 73(1):19-28).

Claims 7-10, 13, 19-21, 29-31, 34 and 35 are drawn to a peptide compound that comprises at least 8 consecutive amino acids of natural hsp70 sequence, wherein the peptide has at least 80% homology with amino acids between 286-294 of natural hsp70, wherein the amino acid at position 293 is chosen from isoleucine, leucine, valine, alanine, glycine, and phenylalanine, wherein the sequence is chosen from SEQ ID No: 1 and 2; a vector expressing a peptide compound; a pharmaceutical compositions comprising peptide compounds, wherein the composition comprises a pharmaceutically acceptable vehicle, seleceted from liposomes, negatively charged liposomes, nanoparticels, and lipid emulsions wherein the composition is compatible with IV, subcutaneous, oral, or nasal administration; wherein the composition comprises at least one immunological adjuvant, and a method of immunization comprising the administration of a peptide compound wherein the peptide comprises at least 8 consecutive amino acids of naturally occurring hsp70 and a peptide which comprises at least 8 consecutive amino acids of hsp70 having at least one mutation with respect to naturally occurring hsp70.

Dragon *et al* does not teach, (see the 35 USC 102 (b) rejection above for Dragon *et al* disclosure) a pharmaceutical compound comprising an adjuvant nor does it disclose a pharmaceutical vehicle.

Prakken *et al* teach the combination of hsp with adjuvants such as Freund's and DDA (see pg 3284-3285, Antigens and Adjuvants of Material and Methods section). Moreover, Prakken *et al* also discloses a compound which is at least 8 amino acids which is to be administered to a subject for the purposes of immunization.

Costa MH *et al* teach the combination of hsp with a suitable pharmaceutical vehicle, wherein the vehicles disclosed are liposomes. Furthermore, Costa MH *et al* disclose the use of hsp-liposome as a vaccine in the generation of an immune response in a subject.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the compound comprising a peptide (comprising at least 8 amino acids from naturally occurring hsp, wherein the composition had a mutation, was at least 80% homologous to naturally occurring hsp, comprised a mixture of peptide compounds, comprised a pharmaceutical vehicle, a compound which is compatible with administration, and methods of immunizing the compound to a subject) with an adjuvant and liposomal vehicles for administration because the compound and method of using the peptide compound where already known in the art and the combination of a known compound with well known additives and accessory items, such as adjuvants and liposomal vehicle molecules, was also well known and widely practiced in the art. One of ordinary skill in the art would have been

motivated to combine the compound and method with adjuvants and liposomal vehicles because adjuvants and vehicles are common ingredients of vaccines to be administered and one of ordinary skill would have expected a reasonable amount of success in combining the compound and method with the adjuvant and liposome because it was well practiced in the art.

Conclusion

No claim is allowed Because of the newly applied rejections, this action is made NON-FINAL.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
September 30, 2002

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